(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) EP 1 159 917 A1

(12) EUROPEAN PATENT APPLICATION

(43) Date of publication:
05.12.2001 Bulletin 2001/49

(51) Int Cl.7: A61B 5/07, A61B 5/00

(21) Application number: 01304793.1

(22) Date of filing: 31.05.2001

(84) Designated Contracting States:
AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE TR
Designated Extension States:
AL LT LV MK RO SI

(30) Priority: 31.05.2000 US 583275

(71) Applicant: Given Imaging Ltd.
Yoqneam 20692 (IL)

(72) Inventor: Glukhovsky, Arkady
Nesher 36790 (IL)

(74) Representative: Smart, Peter John
W.H. BECK, GREENER & CO
7 Stone Buildings
Lincoln's Inn
London WC2A 3SZ (GB)

(54) Apparatus for measuring electrical characteristics of tissue

(57) Apparatus and method for measuring electrical characteristics of biological tissues. The apparatus includes an autonomous capsule (10') with an external surface having openings (21,21'), a plurality of electrodes (20,20',20") located within the openings, and a processor (36) in communication with the plurality of electrodes for generating electrical characteristics such as impedance values or conductivity values.

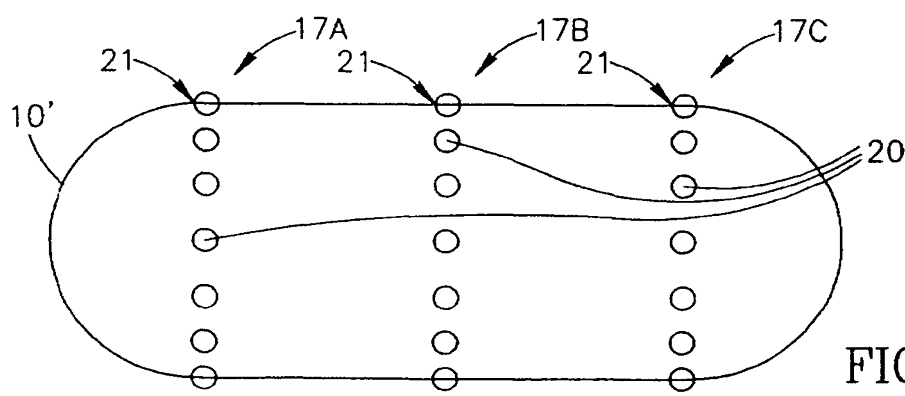

FIG.2A

EP 1 159 917 A1

Printed by Jouve, 75001 PARIS (FR)

BNSDOCID: <EP_____1159917A1_I_>

Description

FIELD OF THE INVENTION

[0001] The present invention relates to *in-vivo* measurement systems in general and specifically to a device for internal measurements of electrical characteristics of a biological lumen.

BACKGROUND OF THE INVENTION

[0002] Physiological tissues are typified by specific electrical impedance characteristics. Variance in types of epithelial tissue, for example, may be recognized by differences in electrical characteristics (Gonzales-Correa CA et al., "Virtual biopsies in Barrett's esophagus using an impedance probe", Annals of NY Academy of Sciences, Vol. 873, April 1999, pp. 313-321).

[0003] Changes of this characteristic impedance can provide essential information about the tissue, and the entire organism. This concept has been the springboard for a great deal of research into predicting pathological conditions, especially cancer (Blad B and Baldetorp B, "Impedance spectra of tumor tissue in comparison with normal tissue: a possible clinical application for electrical impedance tomography", Physiological Measurements, Vol. 17 Suppl 4A, November 1996, pp. 105-115). For example, the early detection of colon cancer may be possible by examining differences in electrical properties of surface colonic epithelium (Davies RJ et al., "Colonic epithelial impedance analysis in a murine model of large-bowel cancer", Archives of Surgery, Vol. 124 (4), April 1989, pp. 480-484). These measurements are generally done using an endoscope or a probe with electrodes at the end.

[0004] Similarly, breast cancer may be predictable based on impedance differences in normal and pathological tissue (Chauveau N et al., "Ex vivo discrimination between normal and pathological tissues in human breast surgical biopsies using bioimpedance spectroscopy", Annals of NY Academy of Sciences, Vol. 873, April 1999, pp. 42-50; and Jossinet J, "A Variability of impedivity in normal and pathological breast tissue, Medical and Biological Engineering and Computing, Vol. 34(5), September 1996, pp. 346-350).

[0005] Many other conditions may be predictable based on electrical impedance changes. For example, esophagus impedance may be related to Barrett's esophagus, a disorder in which the normal squamous mucosa of the esophagus is replaced by columnar epithelium (Gonzales-Correa CA et al., "Virtual biopsies in Barrett's esophagus using an impedance probe", Annals of NY Academy of Sciences, Vol. 873, April 1999, pp. 313-321). Changes in oral impedance may be related to changes in oral mucosa (Nicander BL et al.. "Electrical impedance. A method to evaluate subtle changes of the human oral mucosa", European Journal of Oral Science, Vol. 105(6), December 1997, pp. 576-582). Other diagnoses using this principle include tissue injury (Paulsen KD et al., "In vivo electrical imedance spectroscopic monitoring of the progression of radiated-induced tissue injury", Radiation Research, Vol. 152(1), July 1999, pp. 41-50), lung ventilation (Frerichs I et al., "Monitoring regional lung ventillation by functional electrical impedance tomography during assisted ventillation", Annals of NY Academy of Sciences, Vol. 873, April 1999, pp. 493-505), and ischemic tissue (Casa O et al., "In vivo and in situ ischemic tissue characterization using electrical impedance spectroscopy", Annals of NY Academy of Sciences, Vol. 873, April 1999, pp. 51-58).

[0006] Measurement of impedance characteristics of tissue is typically accomplished through the use of a probe with electrodes or by implanting electrodes (Lehrer AR et al., "Electrical resistance of genital tissues during reproductive events in cows, and its possible on-farm applications: A review", Wiener Tierarztliche Monatsschrift, Vol. 78, 1991, pp. 317-322). The electrodes may be attached to the end of an enteroscope for measurements of the intestines. Additional techniques have been developed as well. One of these techniques is termed "electrical impedance tomography", or EIT (Brown BH et al., "Applied potential tomography: possible clinical applications", Clinical Physiology and Physiological Measurements, Vol. 6(2), May 1985, pp. 109-121). This method involves resistivity distribution changes following ingestion of conducting or insulating fluids. In addition, body composition may be analyzed by total body conductivity (Galvard H, et al., "Differences in body composition between female geriatric hip fracture patients and healthy controls: body fat is a more important explanatory factor for the fracture than body weight and lean body mass", Aging (Milano), Vol. 8(24), August 1996, pp. 282-286; and Yasiu T, et al., " Body composition analysis of cachetic rabbits by total body electrical conductivity", Nutrition and Cancer, Vol. 32(3), 1998, pp. 190-193).

SUMMARY OF THE INVENTION

[0007] The present invention describes an apparatus and method for measuring electrical characteristics of a biological lumen.

[0008] There is thus provided, in accordance with a preferred embodiment of the present invention, an apparatus for measuring electrical characteristics of biological tissues which includes a capsule with an external surface having openings, a plurality of electrodes located within the openings, and a processor in communication with the electrodes for generating electrical characteristics.

[0009] The apparatus may further include an imager for imaging an area of interest within the biological tissue.

[0010] The capsule may be autonomous, and it may be introduced by swallowing or by placing it in a desired location in the body.

[0011] The electrical characteristics may include impedance or conductivity values or any other relevant electrical characteristics as determined by the user. The biological tissue may be the small intestine or the interior of any portion of the digestive tract.

[0012] The plurality of electrodes includes at least two electrodes. Electrodes may be metallic rings, where the openings are slits, or they may be metallic spheres or cups, where the openings are round. Electrodes may protrude through the openings or they may be flush with the external surface of the capsule.

[0013] The invention further describes a method for measuring electrical characteristics of a digestive tract in a body, including the following steps: introducing into the digestive tract an autonomous electrode configuration, selecting sets of electrodes for measurement, introducing a current into the selected electrodes, collecting electrical data from selected electrodes, and calculating electrical characteristics from collected data. The autonomous configuration may be located on the external surface of a capsule, and it may be introduced into the digestive tract by swallowing.

[0014] A further embodiment of the present invention includes the step of transmitting the electrical characteristics to a wireless receiver outside the body.

[0015] In one embodiment of the present invention the step of collecting includes obtaining a voltage between the two selected electrodes. Electrical characteristics may be impedance or conductivity values.

[0016] Furthermore, one embodiment of the present invention includes the step of measuring a time parameter. Another embodiment further includes the step of determining a distance within the digestive tract.

BRIEF DESCRIPTION OF THE DRAWINGS

[0017] The present invention will be understood and appreciated more fully from the following detailed description taken in conjunction with the appended drawings in which:

Fig. 1 is a block diagram illustration of a prior art swallowable capsule for video imaging;
Figs. 2A, 2B and 2C are schematic illustrations of several embodiments of a capsule of the present invention having electrodes thereon;
Fig. 3 is a cross section illustration of the capsule of Fig. 2A within the small intestine;
Fig. 4 is a block diagram illustration of impedance measurement and transmission;
Fig. 5A is a graphical illustration of impedance for two electrodes, useful in understanding the measurement and processing illustrated in Fig. 4; and
Fig. 5B is a graphical illustration of the correlation of the two traces of Fig. 5A.

DETAILED DESCRIPTION OF THE INVENTION

[0018] The present invention is a capsule with external electrodes. It may be autonomous, in that it moves through the digestive system without external control, and it may be introduced into the body by swallowing or by placing it in a desired location in the body.

[0019] In vivo measurement systems which are known in the art typically include swallowable electronic capsules which collect data and which transmit the data to a receiver system. These intestinal capsules, which are moved through the digestive system through the action of peristalsis, are often called "Heidelberg" capsules and are utilized to measure pH, temperature ("Core-temp") and pressure throughout the intestines. They have also been utilized to measure gastric residence time, which is the time it takes for food to pass through the stomach and intestines.

[0020] The intestinal capsules typically include a measuring system and a transmission system, where the transmission system transmits the measured data at radio frequencies to the receiver system. The receiver system is usually located outside the body. Alternate systems can store all the data within a storage device in the capsule. The data can then be read after the capsule exits the gastro-intestinal (GI) tract.

[0021] In US 5,604,531, which is incorporated herein by reference, the common assignees of the present application describe a swallowable capsule that can pass through the entire digestive tract, including the small intestine, and operate as an autonomous video endoscope. A block diagram of the system of US 5,604,531 is illustrated in Fig. 1.

[0022] The *in vivo* video camera system typically comprises a swallowable capsule 10 for viewing inside the digestive system and for transmitting at least video data, a reception system 12 typically located outside a patient, and a data processor 14 for processing the video data. The data processor 14 typically operates two monitors, a position monitor 16 on which the current location of the capsule 10 within the digestive system is displayed and an image monitor 18 on which the image currently viewed by the capsule 10 is displayed.

[0023] The reception system 12 can either be portable, in which case the data it receives is temporarily stored in a storage unit 19 prior to its processing in data processor 14, or it can be stationary and close to the data processor 14. The capsule typically comprises an illumination source 42, an imager 46, and a transmitter 41.

[0024] Reference is now made to Figs. 2A, 2B and 2C, which illustrate several embodiments of a capsule 10' of the present invention having electrodes 20 thereon. It should be noted that the capsule 10' as described with electrodes 20 thereon may or may not additionally comprise the in vivo camera system described above.

[0025] The capsule 10' is typically made from plastic material, and is fabricated with small openings 21 for

electrodes 20. The electrodes 20 are placed through the openings 21 so that part of each electrode 20 remains within the interior portion of the capsule 10', and part of each electrode 20 protrudes out from the other side of the opening 21. Alternatively, electrodes 20 may be flush with the surface of the capsule 10'. The electrodes 20 may be spherical in shape, or they may be fabricated in other shapes and forms, such as cup-shaped electrodes 20' as in Fig. 2B.

[0026] In the configuration illustrated in Fig. 2C, the openings 21' are slits positioned around the capsule 10', within which are located electrodes 20" in the form of metallic rings. In either embodiment, capsules 10' must include a minimum of two electrodes, but may contain many more, in sets of two. Other embodiments are possible as well.

[0027] Reference is now made to Figs. 3 and 4. Fig. 3 is a cross section illustration of the capsule 10' with spherical electrodes 20 within the intestine 22 and Fig. 4 is a block diagram illustration of the processing output of the electrodes.

[0028] As shown in Fig. 3, at any given point in time, some electrodes will be in contact with the interior portion of the digestive tract, while others will not. Impedance values measured between a pair of electrodes which are in contact with the digestive tract will be much higher than ones not in contact. Thus, as shown in Fig. 4, a multiplexer 26 is used to select a pair of electrodes (for example, 20A or 20B (Fig. 3)) for measurement of electrical potential and calculation of impedance, or conversely, conductivity values.

[0029] The circuit of Fig. 4 comprises a current source 24, a multiplexer 26, an analog to digital (A/D) converter 34, a microprocessor 36, and the transmitter 41. Current source 24 sends a known, constant current i_{input} through multiplexer 26, which selects a first pair of electrodes 20A. The resulting voltage V_{output} is converted by A/D converter 34 and provided to microprocessor 36, which calculates an impedance value therefrom. Impedance Z (expressed in Ohms) is calculated as the normalized ratio of voltage to current according to the following equation:

$$Z = L * V_{output}/i_{input}$$

where L is the distance between the selected electrodes.

[0030] The multiplexer 26, in direct communication with microprocessor 36, then selects another pair of electrodes 20B for impedance calculations. Every possible combination of electrode pairs is selected. Microprocessor 36 then selects the maximum impedance value from among the electrode pairs and this value is transmitted through transmitter 41 to a receiver located outside the body. The transmitted value is proportional to a characteristic impedance value for the region being measured, and is used for comparison with values obtained from other regions within the digestive tract. A similar method may be employed for other electrode configurations.

[0031] Measurements may be made at any point along the digestive tract, although the smaller diameter sections will have more contact with the electrodes. Measurements are taken at periodic intervals, for example every 0.1 second. The location of the capsule within the digestive tract at the time of measurement is determined by a telemetric system, as described in US 5,604,531. Changes in impedance may also signal passage of the capsule through different segments of the digestive tract, such as the pylorus or various organs. For example, differences in pH values along the tract, such as the stomach versus the intestines, will result in changes in impedance measurements. These values may also aid the telemetry system of US 5,604,531 in confirming the location of the capsule 10' along the path of the digestive tract.

[0032] Reference is now made back to Fig. 2A, which shows electrodes 20 surrounding capsule 10', in rows 17A, 17B and 17C. Rows 17A, 17B and 17C are separated from one another by known distances, and there may be any number of rows of electrodes 20.

[0033] Reference is now made to Figs. 5A and 5B. Fig. 5A shows the impedance values of two sets of electrodes over time, while Fig. 5B illustrates the cross-correlation of the output of the two sets of electrodes. Due to spatial inhomogeneity of the tissues along the path of the capsule, the measured impedance versus time will show some fluctuations. In the graph, the solid line represents the signal obtained from a first pair of electrodes 20 located along a first row 17A (Fig. 2A). The dotted line represents the signal obtained from another pair of electrodes 20 located along a second row 17B (Fig. 2A). Similar measurements may be made from other electrode configurations. The two resulting traces are similar, but there is a time lag between them.

[0034] Fig. 5B shows the cross-correlation between the two pairs of electrodes located around the capsule. As can be seen, there is a peak 32 in the graph. This peak occurs at time T and indicates the time it takes for the capsule to travel the distance between the two pairs of electrodes. It should be noted that a minimum of four electrodes are needed for this calculation.

[0035] These values can be used to calculate the velocity of the capsule, for example using a method similar to the one described in US 5,116,119, which is incorporated herein by reference. US Patent Number 5,116,119, entitled "Method and Apparatus for Measuring Liquid Flow", describes a method of measuring liquid flow by electromagnetic radiation within a chamber of known dimensions. The momentary attenuation of the electromagnetic radiation by the liquid is measured so as to determine the momentary volume and velocity of the liquid. Similarly, the present invention utilizes electrical properties to determine velocity.

[0036] Other information may also be obtained from

the cross-correlation. For example, the length of a segment from some known reference point, such as the pylorus. can be calculated.

[0037] It will be appreciated by persons skilled in the art that the present invention is not limited by what has been particularly shown and described herein above. Rather the scope of the invention is defined by the claims which follow:

Claims

1. Apparatus for measuring electrical characteristics of biological tissues, comprising:

    a capsule with an external surface having openings;
    a plurality of electrodes located within said openings; and
    a processor in communication with said plurality of electrodes for generating said electrical characteristics.

2. Apparatus according to claim 1 further comprising an imager for imaging an area of interest within said biological tissue.

3. Apparatus according to claim 1 wherein said capsule is autonomous.

4. Apparatus according to claim 1 wherein said capsule is introduced by swallowing or by placing it in a desired location in the body.

5. Apparatus according to claim 1 wherein said electrical characteristics include impedance values or conductivity values.

6. Apparatus according to claim 1 wherein said biological tissue is the small intestine or the interior of any portion of the digestive tract.

7. Apparatus as in claim 1 wherein said plurality of electrodes includes at least two electrodes.

8. Apparatus according to claim 1 wherein said electrodes are metallic rings and said openings are slits or wherein said electrodes are metallic spheres and said openings are round or wherein said electrodes are cup-shaped and said openings are round.

9. Apparatus according to claim 1 wherein said electrodes are flush with said external surface or wherein said electrodes protrude from said external surface.

10. A method for measuring electrical characteristics of a digestive tract in a body, the method comprising the steps of:

    introducing into said digestive tract an autonomous electrode configuration;
    selecting sets of electrodes for measurement;
    introducing a current into said selected electrodes;
    collecting electrical data from said selected electrodes; and
    calculating electrical characteristics from said collected data.

11. A method as in claim 10 wherein said step of introducing is accomplished by swallowing.

12. A method as in claim 10 wherein said electrode configuration is located on an external surface of a capsule.

13. A method as in claim 10 further comprising the step of transmitting said calculated electrical characteristics to a receiver outside said body.

14. A method as in claim 10 wherein the step of collecting includes obtaining a voltage between two said selected electrodes.

15. A method as in claim 10 wherein the step of calculating includes calculating an impedance between two said selected electrodes or calculating conductivity.

16. A method as in claim 10 further comprising the step of measuring a time parameter.

17. A method as in claim 10 further comprising the step of determining a distance within the digestive tract.

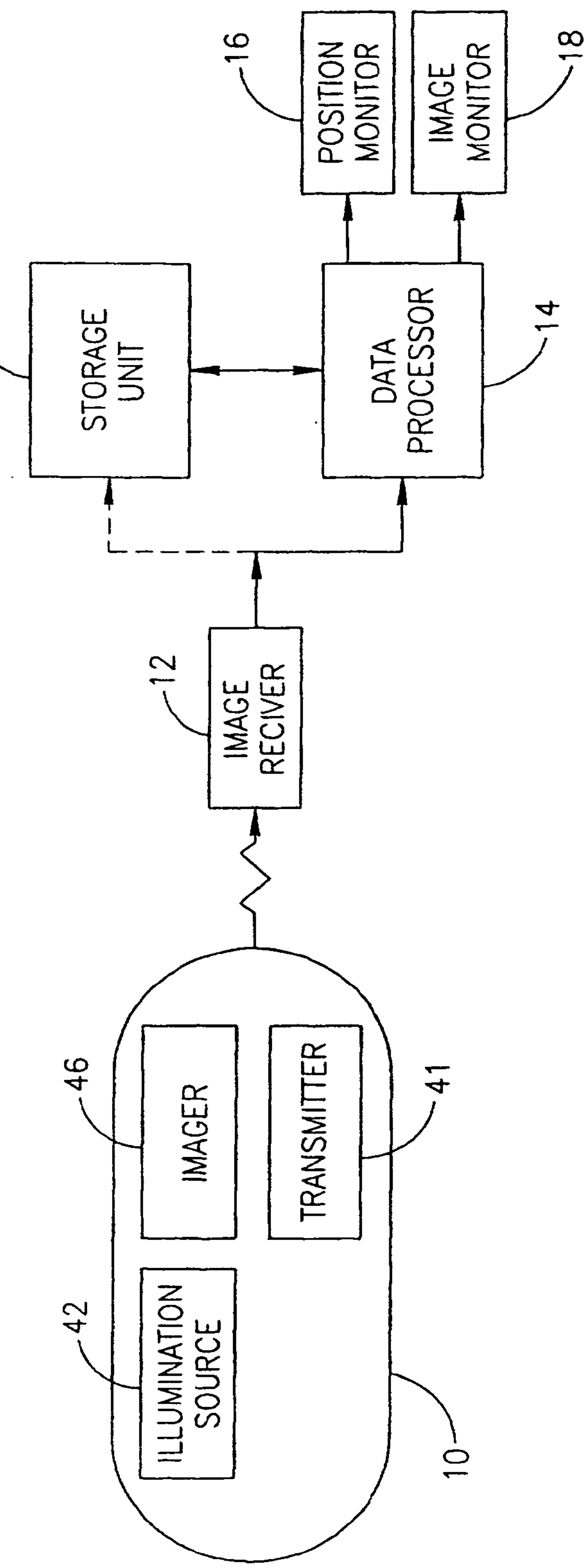

FIG.1
PRIOR ART

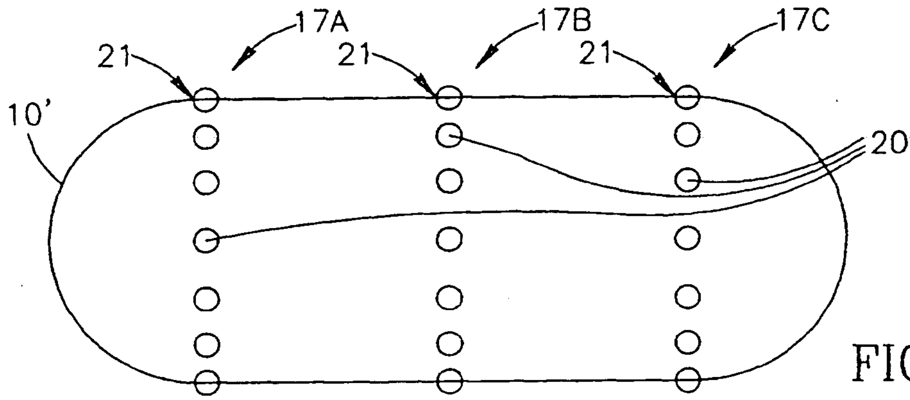

FIG.2A

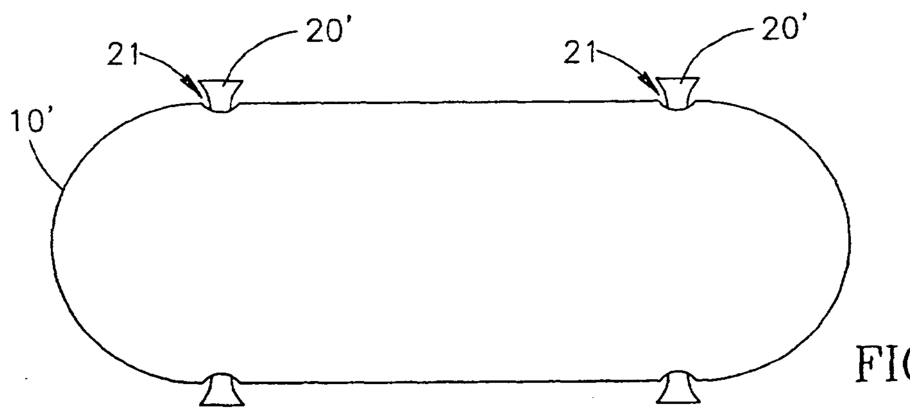

FIG.2B

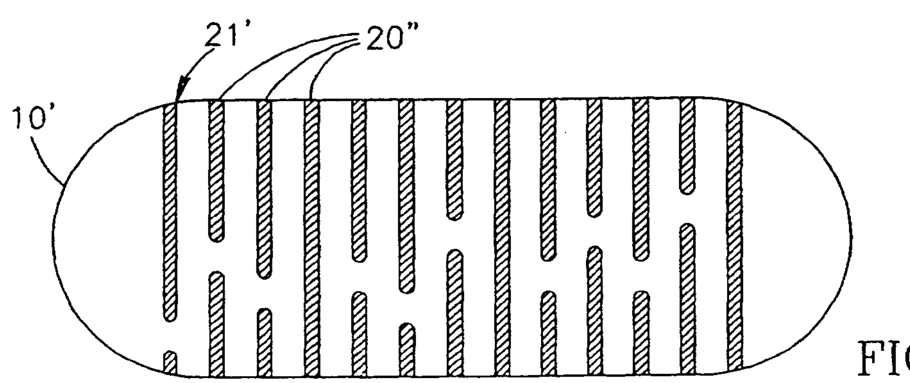

FIG.2C

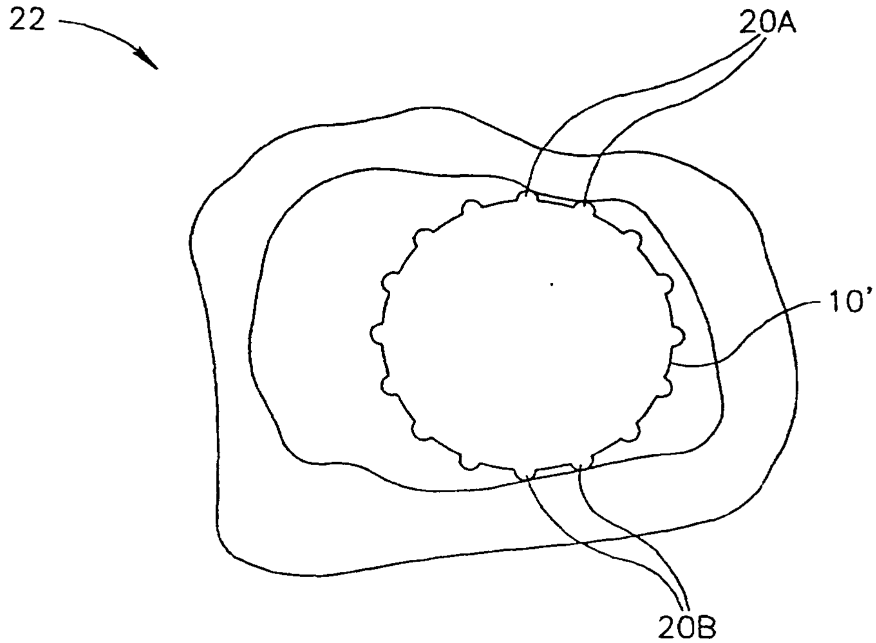
22
20A
10'
20B

FIG.3

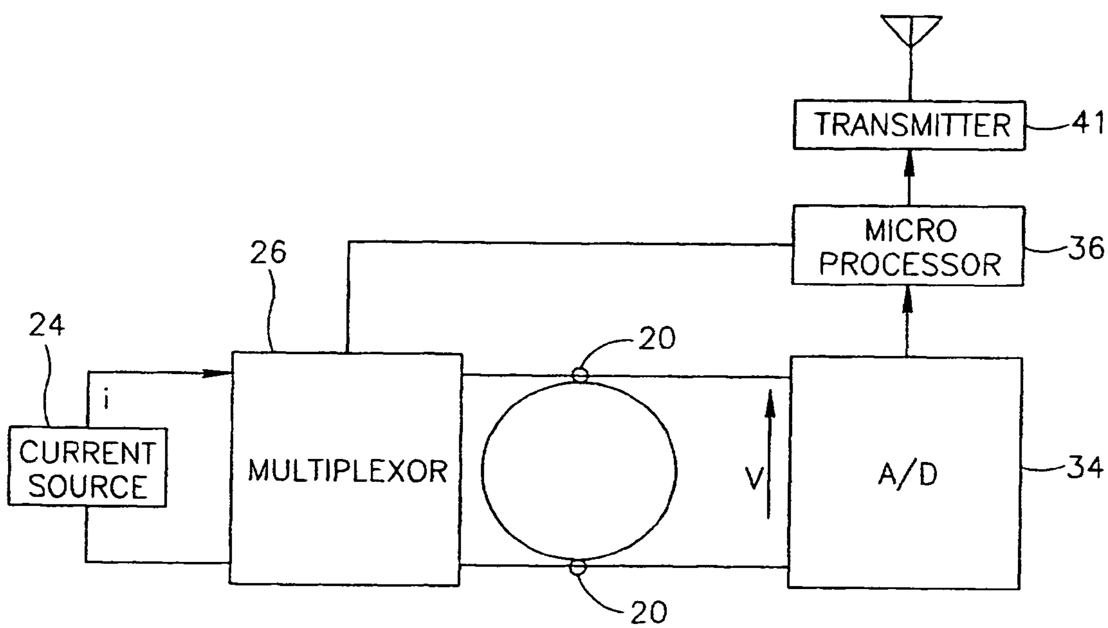
TRANSMITTER
41
MICRO
PROCESSOR
36
26
24
i
20
CURRENT
SOURCE
MULTIPLEXOR
V
A/D
34
20

FIG.4

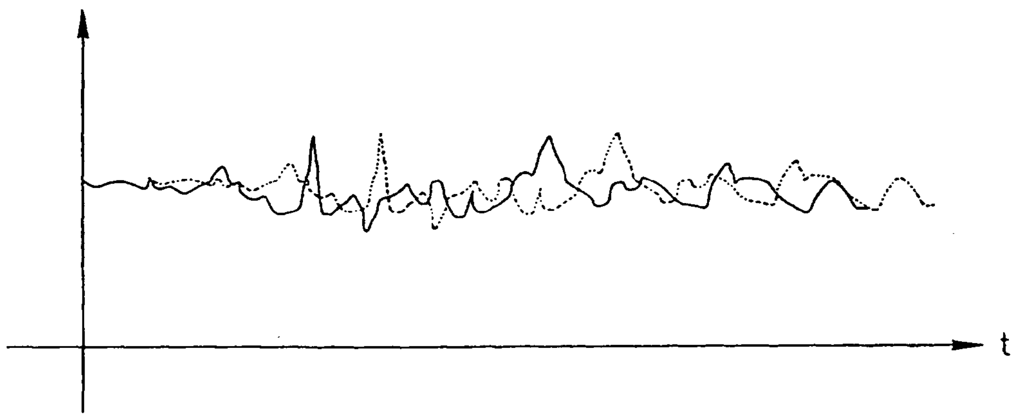

FIG.5A

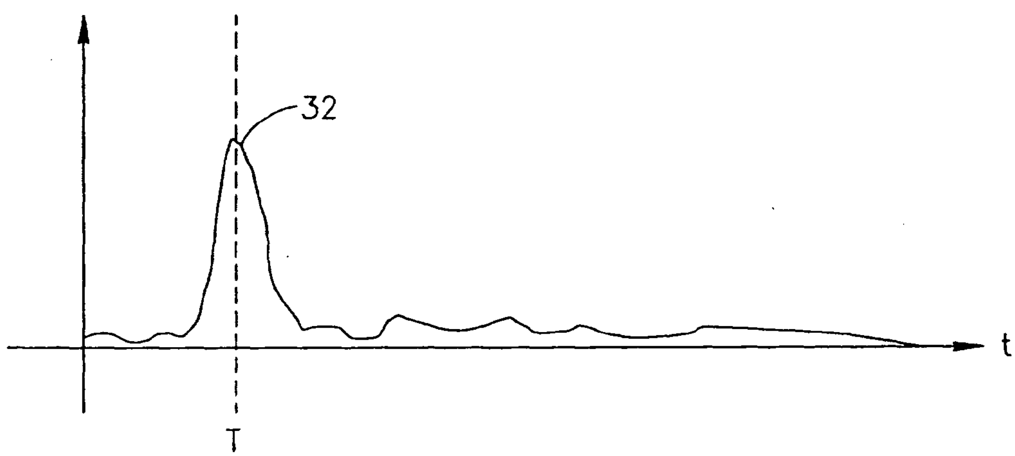

FIG.5B

European Patent Office

PARTIAL EUROPEAN SEARCH REPORT

which under Rule 45 of the European Patent Convention shall be considered, for the purposes of subsequent proceedings, as the European search report

Application Number EP 01 30 4793

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
X Y	DE 29 41 363 A (DEUTSCHE FORSCH LUFT RAUMFAHRT) 30 April 1981 (1981-04-30) * page 3, paragraph 1 - page 5, paragraph 1; figures 1-4 * ---	1,3-9 2	A61B5/07 A61B5/00
X Y	EP 0 344 770 A (ISRAEL STATE ;YEDA RES & DEV (IL)) 6 December 1989 (1989-12-06) * column 5, line 49 - column 10, line 55; figures * ---	1,3-9 2	
X Y	US 4 784 155 A (MILLS PERRY A) 15 November 1988 (1988-11-15) * column 2, line 38 - column 3, line 25; figure 2 * ---	1,3-9 2	
Y,D	US 5 604 531 A (IDDAN GAVRIEL J ET AL) 18 February 1997 (1997-02-18) * abstract; figures 1-6 * -----	2	

TECHNICAL FIELDS SEARCHED (Int.Cl.7)

A61B
A61N
A61K

INCOMPLETE SEARCH

The Search Division considers that the present application, or one or more of its claims, does/do not comply with the EPC to such an extent that a meaningful search into the state of the art cannot be carried out, or can only be carried out partially, for these claims.

Claims searched completely :

1-9

Claims searched incompletely :

Claims not searched :

10-17

Reason for the limitation of the search:

Article 52 (4) EPC - Method for treatment of the human or animal body by surgery

Place of search	Date of completion of the search	Examiner
MUNICH	27 August 2001	Dhervé, G

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

EPO FORM 1503 03 82 (P04C07)

ANNEX TO THE EUROPEAN SEARCH REPORT ON EUROPEAN PATENT APPLICATION NO. EP 01 30 4793

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report.
The members are as contained in the European Patent Office EDP file on
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

27-08-2001

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
DE 2941363 A	30-04-1981	NONE	
EP 0344770 A	06-12-1989	NONE	
US 4784155 A	15-11-1988	NONE	
US 5604531 A	18-02-1997	IL 108352 A EP 0667115 A	29-02-2000 16-08-1995

EPO FORM P0459

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82

This Page is Inserted by IFW Indexing and Scanning Operations and is not part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- ☐ BLACK BORDERS
- ☐ IMAGE CUT OFF AT TOP, BOTTOM OR SIDES
- ☐ FADED TEXT OR DRAWING
- ☐ BLURRED OR ILLEGIBLE TEXT OR DRAWING
- ☐ SKEWED/SLANTED IMAGES
- ☐ COLOR OR BLACK AND WHITE PHOTOGRAPHS
- ☐ GRAY SCALE DOCUMENTS
- ☐ LINES OR MARKS ON ORIGINAL DOCUMENT
- ☐ REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY
- ☐ OTHER: ______________________

IMAGES ARE BEST AVAILABLE COPY.
As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.